Effect of a constant rate infusion of remifentanil hydrochloride on left ventricular systolic and diastolic function in propofol-anesthetized dogs

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OBJECTIVE
To assess the effects of a constant rate infusion (CRI) of remifentanil hydrochloride on left ventricular systolic and diastolic function in healthy propofol-anesthetized dogs.

ANIMALS
6 healthy Beagles.

PROCEDURES
Each dog underwent 2 experimental treatments separated by a 7-day interval. In 1 treatment, anesthesia was induced with propofol and maintained with a CRI of propofol (0.6 mg/kg/min); dogs also received a CRI of saline (0.9% NaCl) solution. In the other treatment, anesthesia was similarly induced and maintained with propofol; dogs also received a CRI of remifentanil (0.3 µg/kg/min). Doppler echocardiographic and hemodynamic variables of interest were determined at baseline (before anesthesia) and at 20, 40, and 60 minutes following the simultaneous start of the 2 CRIs of each treatment; all CRIs were administrated for 60 minutes.

RESULTS
For the 2 treatments, end-diastolic and end-systolic volume indices did not differ from baseline or at any time point. Peak tissue Doppler-derived mitral annulus systolic velocity decreased from baseline with both treatments; however, no differences were found between treatments at any time point. Mean arterial blood pressure decreased similarly with both treatments. Heart rate and Doppler-determined cardiac index decreased significantly with the propofol-remifentanil treatment, compared with findings for the propofol-saline solution treatment. For the propofol-remifentanil treatment, the ratio of peak velocity flow in early diastole to that in late diastole remained > 1.80, whereas the ratio of early to late Doppler-derived mitral annulus velocity had a normal relaxation pattern.

CONCLUSIONS AND CLINICAL RELEVANCE
Results of this study indicated that a CRI of remifentanil administered along with a CRI of propofol does not impair left ventricular systolic and diastolic function in healthy dogs. (Am J Vet Res 2018;79:1261–1267)

ABBREVIATIONS
CRI  Constant rate infusion
CRI-PR  Constant rate infusions of propofol and remifentanil hydrochloride
CRI-PS  Constant rate infusions of propofol and saline (0.9% NaCl) solution
DAP  Diastolic arterial blood pressure
DCI  Doppler-determined cardiac index
DEI  Doppler-determined ejection index
EDV  End-diastolic volume
EDVI  End-diastolic volume index (relative to body surface area)
ESV  End-systolic volume
ESVI  End-systolic volume index (relative to body surface area)
HR  Heart rate
IVRT  Isovolumic relaxation time
MAP  Mean arterial blood pressure
PVRI  Peripheral vascular resistance index
SAP  Systolic arterial blood pressure

During the 1980s, most cardiovascular interventions in humans were performed with the use of opioids administered at high doses. However, because of the drugs’ cumulative effects, recovery from anesthesia was commonly prolonged by respiratory depression. To improve recovery quality and maintain hemodynamic stability and myocardial performance, the ideal opioid drug should not have cumulative effects and should be easily titrated for use in longer procedures according to individual requirements. The pharmacokinetic properties of remifentanil are unique owing to its ester linkage in the molecular structure, which results in a noncumulative effect with rapid onset and short duration, regardless of the duration of continuous rate infusion. In human medicine, remifentanil has been widely used for sedation and anesthesia of patients with critical cardiac...
conditions. In addition to an improvement of recovery from anesthesia, remifentanil provides cardiovascular stability, especially when given by CRI.

Despite the reported safety of the use of remifentanil, HR, arterial blood pressure, and cardiac output can be reduced following administration of the drug. Furthermore, a few studies have revealed that cardiomyocytes can be directly regulated by opioid receptors in the heart, which alter myocardial properties (ie, increased negative inotropic and lusitropic responses).

Echocardiography has been used to investigate changes in myocardial performance caused by treatment with remifentanil. In healthy humans and patients with known cardiac diseases, left ventricular systolic and diastolic functions are not changed by remifentanil administration.

Advancements in veterinary medicine have increased the life expectancy of dogs; elderly dogs with cardiac disease are becoming more common among patients requiring anesthesia. Remifentanil can be an excellent option for such animals, wherein cardiovascular stability is a main goal. Although remifentanil-associated decreases in HR and cardiac output in dogs have been detected, some investigators have found minimal changes of no clinical relevance in dogs treated with the drug. However, to date, there are no published echocardiographic studies of left ventricular systolic and diastolic functions in dogs receiving a CRI of remifentanil, to our knowledge.

The aim of the study reported here was to investigate the effects of a CRI of remifentanil hydrochloride administered along with a CRI of propofol on left ventricular systolic and diastolic function in healthy dogs. We hypothesized that, compared with the effects of a CRI of propofol (administered at a rate of 0.6 mg/kg/min) and a CRI of saline (0.9% NaCl) solution (administered at a rate of 5 mL/kg/h), a CRI of remifentanil (administered at a rate of 0.3 µg/kg/min) and a CRI of propofol (administered at a rate of 0.6 mg/kg/min) would not result in clinically relevant changes in echocardiographic variables reflecting left ventricular systolic and diastolic function in healthy adult dogs.

**Materials and Methods**

**Animals**

Six sexually intact Beagles (2 males and 4 females) were used in the study. The dogs were each 5 years old; their mean ± SD weight was 13.0 ± 2.5 kg. Each dog was considered healthy on the basis of results of a physical examination, CBC, serum biochemical analysis (creatinine concentration and alanine transaminase activity), and echocardiographic and ECG evaluations. The dogs were individually housed in kennels, where they received commercial food twice daily and had access to water ad libitum. The study was approved by the local Animal Usage Ethics Committee (protocol No.2015-00316).

**Study design**

Dogs received each of 2 experimental treatments in random order; the treatment order was determined by means of a raffle. In this crossover design study, dogs received the second experimental treatment 7 days after undergoing the first experimental treatment. The 2 experimental treatments were as follows: CRI-PS (CRI of propofol, 0.6 mg/kg/min; CRI of saline solution, 5 mL/kg/h) and CRI-PR (CRI of propofol, 0.6 mg/kg/min; CRI of remifentanil hydrochloride, 0.3 µg/kg/min).

Prior to each experimental procedure, food was withheld from the dogs for 12 hours and water was withheld for 2 hours. Each dog was allowed to familiarize itself with the laboratory for 30 minutes, after which anesthesia was induced with isoflurane (5% in 100% oxygen) delivered at a flow rate of 5 L/min by use of a face mask until orotracheal intubation was possible. Maintenance of anesthesia was achieved with inhalation of isoflurane (1.5% to 2.0% in 100% oxygen) at a flow rate of 50 mL/kg/min. Rectal temperature was maintained between 36.5°C and 38.5°C with the aid of a warm air blanket throughout each experimental procedure.

A dorsal pedal artery and a cephalic vein were catheterized for direct arterial blood pressure monitoring and drug administration, respectively. Catheters were occluded and filled with saline solution containing heparin. Isoflurane anesthesia was discontinued, and each dog was allowed to recover. A 30-minute period was allowed to elapse following inhalation anesthesia prior to baseline data collection.

After collection of baseline data in awake dogs, anesthesia was induced in each dog with an IV bolus of propofol (7 mg/kg), followed by orotracheal intubation and maintenance of anesthesia with a CRI of propofol (0.6 mg/kg/min). Oxygen was provided at a flow rate of 50 mL/kg/min. Intermittent positive-pressure ventilation was initiated to maintain end-tidal carbon dioxide partial pressure between 35 and 45 mm Hg. For the CRI-PS treatment, the CRI of saline solution was commenced at the same time the CRI of propofol was started. For the CRI-PR treatment, the CRI of remifentanil was commenced at the same time the CRI of propofol was started. For each experimental treatment, the CRI-PS and CRI-PR were administered via the cephalic vein catheter.

Two evaluators (MGM and BMMG) who were unaware of the experimental treatment administered to each dog were responsible for data collection at baseline and at 20, 40, and 60 minutes following the simultaneous start of the 2 CRIs of each treatment. Data collected included HR (determined through detection of pulse waves in a multiparameter monitor); MAP, SAP, and DAP (obtained from the same monitor through a transducer zeroed to heart level); oxygen saturation as measured by pulse oximetry (recorded from the multiparameter monitor); and rectal temperature (measured with a
digital thermometer). The DCI was calculated by use of the following equation:

\[
DCI \left( \frac{L}{min/m^2} \right) = \frac{DEI \left[ mL/m^2 \right] \times FC \left[ beats/min \right]}{1,000}
\]

Peripheral vascular resistance was calculated by use of the following equation:

\[
PVRI \left( \text{dynes•s/cm}^2/\text{m}^2 \right) = \frac{(MAP \left[ \text{mm Hg} \right]/DCI \left[ L/\text{min/m}^2 \right]) \times 80.}
\]

Echocardiographic evaluation

For each dog during each experimental treatment, echocardiography was performed and findings were analyzed by the same person (MGM), who was unaware of the administered experimental treatments. A 1- to 4-MHz multifrequency transducer was used for Doppler echocardiographic evaluation and simultaneous ECG for measurements of various variables, some of which were used for additional calculations. The Doppler echocardiographic variables of interest were determined at baseline (before anesthesia) and at 20, 40, and 60 minutes following the simultaneous start of the 2 CRIs of each treatment.

Left ventricular EDV and ESV were measured in an apical 4-chamber view that was obtained through a modified Simpson method.20,29 The principle underlying this method is that total left ventricle volume is calculated from the summation of a stack of elliptical disks. The left ventricle volumes were measured from an apical 4-chamber view, tracing the left ventricle diastolic and systolic endocardial borders. The echocardiography machine automatically calculated the cavity volumes. These measures were indexed according to body surface area, resulting in values of EDVI and ESVI.30

The peak velocity of early left ventricular filling (ie, the E wave) and atrial contraction (ie, the A wave) were measured in an apical 4-chamber view. In an apical 5-chamber view, aortic time velocity integral and left ventricular ejection time were obtained by means of pulsed Doppler visualization of aortic flow. Isovolumetric relaxation time (the interval from the end of transaortic flow to the beginning of the E wave) was measured with the movable Doppler cursor positioned at a midpoint between left ventricular outflow and transmitral flow.28

The ratio of mitral annulus motion was assessed with tissue Doppler imaging in the apical 4-chamber view. The sample volume was positioned at the lateral margin of the mitral annulus. Two negative peak velocities were measured: one at the time of early left ventricular filling (ie, the E’ wave) and the other at the time of atrial contraction (ie, the A’ wave). An additional positive peak (ie, the S’ wave) was measured at the systolic phase. From these measurements, DEI, DCI, E:A ratio, and E’A’ ratio were calculated.

After data collection at the 60-minute time point, both CRIs were immediately stopped and catheters were removed. Each dog was allowed to recover from anesthesia. Until recovery was complete, rectal temperature, HR, and respiratory rate were monitored.

Statistical analysis

Data for all variables had normal distributions as determined by use of the Shapiro-Wilk test. Group comparisons were performed with a 2-way ANOVA for repeated measures followed by a Tukey test for multiple comparisons. In-group comparisons were performed with a Dunnett test to pair data at each time point with baseline data. Differences were considered significant at a value of \( P < 0.05 \). Analyses were performed with statistical software.1

Results

For all 6 dogs, physiologic, Doppler echocardiographic, and hemodynamic variables of interest were determined at baseline (before anesthesia) and at 20, 40, and 60 minutes following the simultaneous start of the 2 CRIs of each experimental treatment (Tables 1 and 2). Among the dogs, mean HR decreased (approx 32% reduction from baseline) significantly only with the CRI-PR treatment. Compared with baseline values, SAP, DAP, and MAP decreased 33%, 33%, and 34%, respectively, with the CRI-PS treatment and 40%, 45%, and 42%, respectively, with the CRI-PR treatment. There were no differences in these variables between experimental treatments at any time point. With both treatments, the DEI decreased by 17% from baseline; DCI decreased from baseline by 37% with the CRI-PR treatment, but there was no significant change with the CRI-PS treatment. At the 20-, 40-, and 60-minute time points, DCI differed significantly between experimental treatments. With the CRI-PS treatment, PVRI was significantly decreased at the 60-minute time point, compared with the baseline.

With both treatments, EDVI and ESVI did not differ from baseline at any time point and there were no significant differences between treatments (Table 1). Peak systolic S’ wave decreased with both treatments, compared with baseline values; however, no differences between treatments were evident at any time point. The E wave decreased from baseline with both treatments (Table 2). For the A wave, mean percentage reduction from baseline with the CRI-PS and CRI-PR treatments was 30% and 40%, respectively. The E:A and E’A’ ratios were compared to expected values for dogs (1 ≤ E:A ratio ≤ 1.80; E’A’ ratio, ≥ 1).28 When dogs received the CRI-PS treatment, the E:A ratio remained within the expected range; when dogs received the CRI-PR treatment, there was an increase (E:A ratio, ≥ 1.80) at the 20-minute time point, which persisted until the 60-minute time point. The E’A’ ratio was similar with both treatments, and values remained within the accepted limits. With the CRI-PS treatment, the IVRT increased significantly, compared with baseline, at all time points. With the CRI-PR treatment, the IVRT increased significantly, compared with baseline, at the 40- and 60-minute time
points. There were no differences in IVRT between experimental treatments.

Discussion

To our knowledge, this was the first study to investigate echocardiographic variables during remifentanil infusion in healthy propofol-anesthetized dogs. Unlike other studies that involved only invasive methods of hemodynamic monitoring, the present study allowed us to investigate intrinsic systolic and diastolic characteristics of the heart echocardiographically, thereby enabling evaluation of the actions of remifentanil combined with propofol on myocardial dynamics in healthy dogs. Furthermore, echocardiography is a noninvasive technique that has low risk for patients and provides real-time information about the cardiac cycle, allowing more precise analyses. The results of the present study in dogs indi-

Table 1—Echocardiographic and hemodynamic variables assessed in 6 healthy Beagles before anesthesia (baseline) and at intervals after the start of experimental CRI-PS or CRI-PR treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>Baseline</th>
<th>20 minutes</th>
<th>40 minutes</th>
<th>60 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>CRI-PS</td>
<td>113 ± 24</td>
<td>101 ± 18</td>
<td>101 ± 19</td>
<td>101 ± 18</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>111 ± 23</td>
<td>75 ± 13‡</td>
<td>74 ± 13‡</td>
<td>74 ± 14‡</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>CRI-PS</td>
<td>144 ± 27</td>
<td>97 ± 19a</td>
<td>100 ± 10a</td>
<td>100 ± 12a</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>156 ± 30</td>
<td>93 ± 7a</td>
<td>95 ± 9a</td>
<td>93 ± 12a</td>
</tr>
<tr>
<td>DAP (mm Hg)</td>
<td>CRI-PS</td>
<td>82 ± 12</td>
<td>55 ± 7a</td>
<td>52 ± 9a</td>
<td>53 ± 6a</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>82 ± 10</td>
<td>45 ± 2a</td>
<td>43 ± 3a</td>
<td>44 ± 4a</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>CRI-PS</td>
<td>103 ± 10</td>
<td>68 ± 7a</td>
<td>67 ± 8a</td>
<td>66 ± 6a</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>97 ± 6</td>
<td>57 ± 2a</td>
<td>56 ± 4a</td>
<td>57 ± 5a</td>
</tr>
<tr>
<td>EDVI (mL/m²)</td>
<td>CRI-PS</td>
<td>47.6 ± 6.4</td>
<td>42.3 ± 2.5</td>
<td>41.5 ± 3.7</td>
<td>40.7 ± 5.6</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>44.9 ± 9.5</td>
<td>40.6 ± 6.9</td>
<td>44.1 ± 7.9</td>
<td>42.0 ± 5.9</td>
</tr>
<tr>
<td>ESVI (mL/m²)</td>
<td>CRI-PS</td>
<td>10.8 ± 2.3</td>
<td>13.3 ± 2.1</td>
<td>12.8 ± 2.7</td>
<td>12.0 ± 2.6</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>11.2 ± 3.1</td>
<td>12.1 ± 2.1</td>
<td>14.5 ± 4.1</td>
<td>11.8 ± 1.8</td>
</tr>
<tr>
<td>S’ wave (m/s)</td>
<td>CRI-PS</td>
<td>0.15 ± 0.03</td>
<td>0.10 ± 0.01*</td>
<td>0.12 ± 0.02*</td>
<td>0.11 ± 0.01*</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>0.14 ± 0.02</td>
<td>0.10 ± 0.02*</td>
<td>0.10 ± 0.01*</td>
<td>0.10 ± 0.02*</td>
</tr>
<tr>
<td>DEI (mL/beat/m²)</td>
<td>CRI-PS</td>
<td>46.54 ± 2.01</td>
<td>37.15 ± 5.44</td>
<td>39.26 ± 5.38</td>
<td>38.79 ± 2.88</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>48.59 ± 4.94</td>
<td>40.21 ± 5.26</td>
<td>40.14 ± 3.07</td>
<td>41.75 ± 3.64</td>
</tr>
<tr>
<td>DCI (L/min/m²)</td>
<td>CRI-PS</td>
<td>4.41 ± 0.79</td>
<td>3.74 ± 0.86</td>
<td>3.93 ± 0.92</td>
<td>4.09 ± 0.79</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>4.75 ± 0.87</td>
<td>2.99 ± 0.74</td>
<td>2.98 ± 0.64</td>
<td>2.85 ± 0.64</td>
</tr>
<tr>
<td>PVRI (dyne•s/cm⁵/m²)</td>
<td>CRI-PS</td>
<td>1,895 ± 198</td>
<td>1,546 ± 536</td>
<td>1,441 ± 461</td>
<td>1,352 ± 384</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>1,713 ± 319</td>
<td>1,604 ± 370</td>
<td>1,548 ± 285</td>
<td>1,558 ± 449</td>
</tr>
</tbody>
</table>

Data are reported as mean ± SD.

Each dog underwent the 2 experimental treatments (7-day interval) in random order. For the CRI-PS treatment, anesthesia was induced with propofol and maintained with a CRI of propofol (0.6 mg/kg/min); dogs also received a CRI of saline (0.9% NaCl) solution. For the CRI-PR treatment, anesthesia was similarly induced and maintained with propofol; dogs also received a CRI of remifentanil (0.3 µg/kg/min). For each treatment, the 2 CRIs were started simultaneously. During anesthesia, physiologic, Doppler echocardiographic, and hemodynamic variables of interest were determined.

*For a given treatment, value is significantly (P < 0.05) different from baseline. †Value is significantly (P < 0.05) different (Tukey test) from that for the CRI-PS treatment. S’ wave = Peak tissue Doppler-derived mitral annulus systolic velocity.

Table 2—Echocardiographic variables of left ventricular diastolic function assessed in 6 healthy Beagles before anesthesia (baseline) and at intervals after the start of experimental CRI-PS or CRI-PR treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>Baseline</th>
<th>20 minutes</th>
<th>40 minutes</th>
<th>60 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>E wave (m/s)</td>
<td>CRI-PS</td>
<td>1.00 ± 0.15</td>
<td>0.74 ± 0.09a</td>
<td>0.73 ± 0.09a</td>
<td>0.71 ± 0.07a</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>0.91 ± 0.05</td>
<td>0.73 ± 0.11a</td>
<td>0.72 ± 0.07a</td>
<td>0.70 ± 0.09a</td>
</tr>
<tr>
<td>A wave (m/s)</td>
<td>CRI-PS</td>
<td>0.71 ± 0.007</td>
<td>0.51 ± 0.03a</td>
<td>0.54 ± 0.08a</td>
<td>0.44 ± 0.12a</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>0.63 ± 0.09f</td>
<td>0.35 ± 0.09f</td>
<td>0.39 ± 0.09f</td>
<td>0.39 ± 0.10f</td>
</tr>
<tr>
<td>E:A ratio</td>
<td>CRI-PS</td>
<td>1.40 ± 0.08</td>
<td>1.46 ± 0.17</td>
<td>1.37 ± 0.15</td>
<td>1.47 ± 0.17</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>1.47 ± 0.24</td>
<td>2.16 ± 0.43</td>
<td>1.90 ± 0.31</td>
<td>1.84 ± 0.32</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>CRI-PS</td>
<td>48 ± 7</td>
<td>54 ± 3a</td>
<td>56 ± 6a</td>
<td>59 ± 6a</td>
</tr>
<tr>
<td></td>
<td>CRI-PR</td>
<td>49 ± 6</td>
<td>51 ± 3</td>
<td>53 ± 4a</td>
<td>54 ± 3a</td>
</tr>
</tbody>
</table>

Data are reported as mean ± SD.

A wave = Peak velocity of late left ventricular slow filling. E wave = Peak velocity of early left ventricular filling. E:A ratio = E wave-to A-wave ratio. E’A’ ratio = E’ wave (at time of early left ventricular filling)-to-A’ wave (at the time of atrial contraction) ratio.

See Table 1 for key.
cated that administration of remifentanil along with propofol did not affect systolic and diastolic function of the left ventricle over a 60-minute period.

In the dogs of the present study, propofol administered via CRI at a rate of 0.6 mg/kg/min did not cause significant changes in HR. The commonly reported reduction of baroreflex activity caused by propofol can vary with administration rate. However, when dogs received propofol and remifentanil, there was a notable reduction in HR, compared with baseline. In previous studies of dogs, bradycardia has been detected with the use of remifentanil alone or in combination with propofol. Opioid agents with high affinity for μ-opioid receptors link to receptors in the central vagal sensory nuclei, which in turn increases parasympathetic tone. However, the negative chronotropic effects of propofol and remifentanil are proportional to administration rate; thus, in the present study, remifentanil administered at a rate of 0.5 µg/kg/min combined with propofol administered at a rate of 0.6 mg/kg/min decreased HR. During remifentanil and propofol administration, careful monitoring of HR is important because bradycardia can decrease cardiac output and arterial blood pressure, as illustrated by the results of the present study. These effects were evident when the study dogs received the CRI-PR treatment and DCI and MAP decreased, compared with baseline values. Although the combination of remifentanil and propofol can induce hemodynamic changes, the study dogs had no episodes of severe bradycardia or hypotension requiring treatment, and MAP was maintained at approximately 60 mm Hg, which is within acceptable limits for anesthetized dogs. Results of the present study corroborated those of another study in which the combination of propofol and remifentanil changed arterial blood pressure, although mean values remained > 60 mm Hg.

In the present study, EDVI and ESVI derived from the Simpson planimetric method were used to evaluate left ventricular systolic function. Unlike the geometric method, this technique is more appropriate for dogs because it considers ventricular length. With regard to ESVI, there were no differences among time points or between treatments; therefore, the combination of propofol and remifentanil did not impair left ventricular systolic function. This finding was similar to that of a study performed in humans, in which the combination of these 2 drugs decreased HR, MAP, and DCI. No influence on systolic function indices was evident, however. Furthermore, in other studies, left ventricular systolic function remained stable with the administration of remifentanil in healthy and ill humans. However, it is known that the effects of remifentanil and propofol are dose dependent; therefore, cardiovascular stability is most likely related to infusion rate. The same has been demonstrated previously with CRIs of remifentanil administered at 0.3 or 0.4 µg/kg/min. In the present study, ESVI remained unchanged and within the reference range for dogs, thereby indicating that propofol and remifentanil at the studied infusion rates did not induce changes in the myocardial dynamics of healthy dogs. Similarly, some authors have demonstrated that remifentanil does not change cardiac contractility, which was corroborated by the results of the present study although an opioid infusion alone was not evaluated.

The maximal systolic S’ wave velocity of the mitral annulus was used to assess longitudinal systolic function in the dogs of the present study. Longitudinal myocardial fibers are known to be affected earlier, before any other change happens to radial or circumferential fibers. The results of the present study indicated that S’ wave velocity decreased from baseline with both experimental treatments, but there was no difference between treatments. Therefore, the S’ wave changes were most likely related to the negative inotropic effects of propofol, and the coadministration of remifentanil likely did not change the S’ wave velocity. As previously described, propofol can act on calcium channels and β-adrenoceptors in cardiac muscle, resulting in decreased contractility. Similarly, there are 2 reports of decreases in S’ wave velocity and other echocardiographic indexes in propofol-anesthetized humans. Despite the reduction in S’ wave velocity observed in the dogs of the present study, the S’ wave velocity remained at approximately 0.10 m/s with both treatments. Findings of a previous study in humans indicated that only an S’ wave velocity < 0.8 m/s is suggestive of left ventricle systolic dysfunction. Therefore, we concluded that remifentanil did not impair left ventricular systolic longitudinal function in the propofol-anesthetized dogs of the present study.

Transmitral flow, as well as tissue motion variables, was also assessed to investigate the effects of remifentanil on left ventricular diastolic function. Diastolic dysfunction can precede systolic dysfunction in clinical scenarios and assessment of these variables is important when studying left ventricular function.

In the present study, the decreases in E and A waves can be explained by the effects of the drugs on cardiovascular function. Decreases in arterial blood pressure can result in reduced central venous pressure and venous return, which would in turn attenuate the pressure gradient from the left atrium to the left ventricle. However, the A wave velocity was lower at the 20- and 40-minute time points when dogs received the CRI-PR treatment, compared with findings when they received the CRI-PS treatment; this was likely attributable to the dogs’ lower HR when the CRI-PR treatment was administered, which allowed longer relaxation time and more pronounced early filling (E wave), compared with atrial contraction (A wave).

The reduction of the A wave when dogs received the CRI-PR treatment resulted in an E:A ratio > 1.80 at each time point. These results were compatible with restrictive diastolic dysfunction. However, the E:A’ ratio obtained by means of pulsed
tissue Doppler echocardiography revealed a normal pattern, indicating that diastolic dysfunction did not occur in these dogs. Therefore, pulsed tissue Doppler imaging was fundamentally important when assessing diastolic function. Similar results for humans receiving only remifentanil infusions have been reported, indicating that this opioid agent does not influence echocardiographic relaxation variables of the left ventricle.

Both propofol alone and propofol combined with remifentanil caused an increase in IVRT in the dogs of the present study. Increased IVRT in propofol-anesthetized humans has been reported. However, the physiologic mechanisms responsible for these effects have not yet been elucidated. In the present study, values of IVRT remained within the reference range for dogs with preserved ventricular relaxation, despite the detected treatment-related increases. In another study in humans, a lack of influence of a remifentanil infusion on IVRT was detected.

The main limitation of the present study was the inclusion of only healthy dogs in the experiment; therefore, the applicability of the findings to ill dogs is not known. Furthermore, echocardiography in this study only allowed assessment of global left ventricular function. The use of novel techniques would allow segmental examination of myocardial dynamics, thereby improving the understanding of opioid interactions in the heart. However, results of the present study did indicate that treatment with remifentanil along with propofol does not impair echocardiographic indexes of left ventricular systolic and diastolic function in healthy dogs.

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Footnotes

a. Ulitiva, 5 mg, GlaxoSmithKline Brazil Ltd, São Paulo, Brazil.
b. Warm air blower unit TC3000, Gaymar Industries, Orchard Park, NY.
c. Syringe pump BOSS 200, Biosensor, São Paulo, Brazil.
d. Cardiocap 5, Datex Ohmeda, Helsinki, Finland.
e. MyLab 30 Gold VET, Genova, Italy.

References

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